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THE AMERICAN
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VOL. 102 MARCH, 1930 NO. 3

EDITORIAL

THE AGE OF HOKUM

OUR FAVORITE EVENING newspaper has again broken out in a rash. Tonight it carries in oddly assorted print packages the blatant claims of a dozen or so patent medicine swindles.

Generally speaking a conservative news-sheet—it seems to grow tired of its wonted decency—and every so often goes off on a spree.

Tonight is one of its spree nights and here is a true recital of its orgy of shame. Girth control motivates two of its broadcasting lay-outs.

"Lose weight where you most want to." That is the claim of one advertised product and what a delicate sense of anatomic geography this slogan suggests. This is another ridiculous bit of copy:

> 1930 Belles are not fat—This great change [to modern slender styles] started when science discovered the chief cause of obesity—This factor was embodied in Hokum prescription tablets. People have used them for over 20 years—millions of boxes of them. That is one great reason for the slender figures you see everywhere today—Simply take four tablets daily until weight comes down to normal.

"*Simply* take four tablets"—and the inspired copy-writer must have known that his copy was meant for simpletons.

A red-ray lamp is also pictured as the health-restorer *par excellence.*

"Entirely unlike the damaging ultra-violet or X-ray. Positively cannot burn or blister." Now this particular red-ray lamp emits the ordinary heat rays that an electric toaster—or a red-hot dish of macaroni emit—and to compare it with the ultra-violet lamp or the X-ray is about as reasonable as comparing ginger with dynamite.

Yeast is good for the chest—the medicine chest. Once a chef—now a doctor—and with credentials from geheimrats and physicians-in-waiting to queens and ten-spots, yeast leaves the kitchen for the medicine kit.

A mouth wash graduates to halitotic eminences with one breath—and with another becomes an eradicator of stationary dandruff. No doubt its next achievement will be as a paralytic to the perpendicular proclivities of the non-stationary kind of dandruff.

The athletic foot vies with parrot-fever as a newly discovered advertising malady—and the fear that four out of five may have It, vanishes with our eagerness to "remove the film."

Elsewhere is spread the lying message of a new star on the hokum firmament—a panacea that challenges the medical dictionary to name any disease which it will fail to cure. The faces of low-priced and lower-principled (alleged) physicians adorn the copy. They testify to its marvels in words they never had the intelligence to voice or understand.

And people who run and read—read and run to the nearest shop to beg and buy a bottle.

Truly there is a renaissance of credulity and ignorance if the evening paper is a proper sign—and if the *alarming* sale of these atrocious swindles is any indication.

The age of hokum is here and now.

IVOR GRIFFITH.

SELECTED EDITORIAL

THE DRUG STORE*

THERE IS RIGHTLY the highest esteem and trust for the ancient and honorable calling of the apothecaries. Thus, when the modern brethren of these faithful servants of the public, the pharmacists, have the question put to them by some of their own guild, whether they are not going after strange gods in these days of business expansion, we listen with interest and respect. We appreciate the jealousy expressed regarding conserving the honorable traditions of the cen-

*Reprinted from *Newark Sunday Call.*

turies, but confess at the same time inability to discern the dangers some learned pharmacists proclaim.

The drug-store—that is purely an American name which custom prevents us discarding—is an institution of this country, developed by ourselves, essentially democratic, and, aside from any business considerations, contributing importantly to public health and general welfare. The druggist is one of the few persons in the body civic that everyone believes and trusts. Around this faith has grown the atmosphere of a community personality which even the chain pharmacy has been unable to destroy. In neighborhoods away from commercial centers, the drug-store not only has maintained but has extended its eminence as a personal and private possession of each of its customers. Safeguarded by laws and regulations of their own advocacy, druggists occupy a position of minor priesthood and the faith is not misplaced.

The introduction of such things as soda water, candies, restaurant service, books, cutlery, photographic supplies, tobacco, stationery, and things similarly far removed from medicine, is not alone the result of economic pressure. True it is that pharmacies would rapidly disappear if dependent upon prescription income alone and that many such important branches of the business are practically service at a loss, but it is also true that the institutional developments are the product of demands by the American people. When a drug-store does something that the public does not like, it will hear from it quick enough. That is because every one tells his troubles to a druggist, who knows and keeps enough secrets to wreck a community's peace.

A few years ago a movie was produced in which a great star failed simply because the scenario told of a druggist who sold bad securities to his customers. Not even the fact that he made full and honorable restitution saved the piece. The public didn't like it because it attacked one of its cherished faiths. We do not see any abatement in this popular confidence, though we honor those of the New Jersey profession who have voiced fears lest this regard be lessened.

ORIGINAL ARTICLES

THE RELATION OF THE CHEMICAL INDUSTRY TO PHARMACY

By J. C. Carlin*

THE RELATION of certain branches of the chemical industry to pharmacy and, especially, pharmaceutical manufacture, is quite intimate, and many interests in common exist, as is evidenced by the fact that the pharmaceutical industry depends in many instances for its basic or raw materials on various branches of the chemical industry.

The writer during his experience of over twenty-five years in pharmaceutical and chemical research and manufacture has watched and studied the growth of both of these industries, and it is very interesting to note the number of chemicals produced by large industrial chemical manufacturers that serve as the starting point or raw material in pharmaceutical manufacture.

To go back into history, it is a well-known fact that many important chemical discoveries were made by pharmacists of "the old school" in the so-called apothecary shops of their day and these same discoveries were the bases for many others contingent thereon, and paved the way, in numerous instances, for many industrial chemical developments. These diligent workers are mentioned all through pharmaceutical and chemical literature for over one hundred years, and outstanding among them are the names of such men as Rouelle, Baume, Derosne, Sequin, Scheele, Sertürner, Caventou, Pelletier, Tanret, etc.,[1] and in more recent times, Power, Tschirsch, Squibb, Proctor, Grahame, Diehl, etc. We cannot but wonder with amazement at the pioneer work done by many of the former with the meager knowledge and equipment they had at their command, probably little dreaming that their efforts would be so far reaching and the profession they loved so well would grow to such tremendous proportions as we see today in many large pharmaceutical and chemical manufacturing establishments in which the relationship has grown more intimate and interdependent. During this period many chemical discoveries that have revolutionized medical treatment have been brought about

*Chemical Director, Tennessee Products Corporation, Nashville, Tenn.

[1] LaWall, "Four Thousand Years of Pharmacy."

by pharmaceutical and chemical research, and many new products that are of great value have been added to the pharmaceutical category, such as the synthetic organics derived from coal tar, biologic products and products of catalytic reactions, many of which are used in the original state or in pharmaceutical preparations. This is another indication of the vast strides made in pharmaceutical practice brought about by the tireless efforts of the workers in pharmaceutical and chemical research.

Twenty-five years ago, it was not uncommon to see large pharmaceutical manufacturers producing many of the chemicals required for their own use, as well as supplying them to the trade, and, in some instances, heavy chemicals were also manufactured for sale.[2] This practice has changed somewhat, and today we have many concerns specializing in the manufacture of fine pharmaceutical chemicals, while others devote their efforts to the production of heavy industrial chemicals, both of which find their way into pharmaceutical preparations.

As a further example of the intimate bond of relationship existing between the large industrial chemical producer and the pharmaceutical manufacturer, the writer believes it will be of interest to make specific mention of some of the products manufactured by the corporation with which he is connected that serve as the raw material in the manufacture of many pharmaceutical products.

Let us consider first the products of hardwood distillation. It is well known that the products derived from the destructive distillation of the hardwoods are: Methanol (methyl alcohol), solvents, acetic acid, acetate of lime, charcoal, wood oils, and pitch.

In the case of methanol, after it is properly refined by chemical treatment and fractional distillation (continuous process), the pure methyl alcohol is the basic or raw material for the manufacture of formaldehyde, by the well-known oxidation process, in which metallic platinum, silver, or copper is used as a catalyst, silver, or copper being used mostly on account of cost. The oxidation is represented by the following equation: $CH_3OH + O = HCHO + HOH$. The process is not quantitative in yield as only about 65 per cent. of the methyl alcohol is oxidized on one pass through the equipment, but the unoxidized alcohol is recovered by distillation and used again, so that a yield approaching the theoretical is obtanied. Paraformaldehyde, a

[2] Experienced by the writer.

solid polymeride $(CH_2O)_6H_2O$ of formaldehyde is another derivative and is formed when an aqueous solution of formaldehyde is allowed to evaporate slowly. It is quite interesting to note here, that if the paraformaldehyde is heated it is converted into another polyoxymethylene, *i. e.,* metaformaldehyde, which melts at 171° and again reverts to gaseous formaldehyde CH_2O. Hexamethylenetetramine (methenamine), another well-known pharmaceutical chemical is made from formaldehyde by reaction with ammonium hydroxide, or neutral ammonium salts as expressed by the following equations:

$$4\ NH_4OH + 6CH_2O = (CH_2O)_6N_4 + 10H_2O \text{ and}$$
$$4\ NH_4Cl + 6CH_2O = (CH_2O)_6N_4 + 4HCl + 6H_2O$$

Methyl alcohol also finds wide use as a solvent and is used in the semi-refined state as a denaturant for ethyl alcohol as in denatured alcohol formula No. 1 which is authorized for use in the extraction of drugs and manufacture of many pharmaceutical preparations.[3] It is also one of the raw materials used in the manufacture of methyl salicylate (artificial oil of wintergreen) by the following reaction, the sulphuric acid acting as the catalyst

$$CH_3OH + C_6H_4OH.COOH + H_2SO_4 = C_6H_4OH.COOCH_3 + H_2O + H_2SO_4$$

Acetate of lime has been for many years the chief commercial source of acetic acid, although the acetic acid occurs in the pyroligneous acid (or liquor) originally and is recovered as acetate of lime. The acetate is decomposed with sulphuric acid and the acetic acid recovered by distillation, treated chemically and redistilled. This has been the method in vogue for many years, but other more direct methods are being devised and acetic acid is now produced in considerable quantity by direct extraction from the pyroligneous liquor by immiscible solvents: as for instance in the Brewster process, using a light boiling solvent like ethyl ether by counter-current extraction (cold), and by the Suida process, using high boiling solvents such as wood oils boiling at 150° C. and over. This process is also based on the counter-current principle, but extraction is made in the vapor phase, hot. In processes of this kind, after extraction, the acid is purified if necessary and

[3] See U. S. Government regulations covering uses of Denatured Alcohol.

concentrated by further distillations. Several other similar processes are in use in Europe, but are more or less in the experimental stage. A catalytic process is also now being used, based on the production of acetaldehyde from acetylene and subsequent oxidation as expressed by the following two-step equation:

$$(1)\ CH : CH + H_2O = CH_3CHO$$
$$(2)\ CH_3CHO + O = CH_3COOH$$

The first step is carried out by passing the gas into sulphuric acid of various concentrations (usually 6 per cent.), and using mercury as the catalyst, the aldehyde being removed by distillation or an appropriate solvent.

The second step is carried out by dissolving the aldehyde in glacial acetic acid, using a manganese salt as the catalyst when rapid oxidation to acetic acid takes place.

Direct production of acetic acid from acetylene is also possible according to the following reaction:

$$CH : CH + H_2O + O = CH_3COOH$$

The acetylene is passed through a solution of persulphuric acid or hydrogen peroxide, using mercury as a catalyst.

Acetic acid occupies a prominent place in pharmacy as it is a raw material in the manufacture of all the U. S. P. acetates and is used in acetic menstruums in drug extraction. It is also used in the production of esters for flavoring purposes and in the preparation of organic acetyl derivatives such as acetanilid, phenacetine, acetyl salicylic acid, etc.

At this point acetone, so well known in pharmaceutical practice, a derivative of acetic acid, should receive mention, not only for its wonderful miscibility and solvent properties, but also because it is a raw material used in the manufacture of chloroform, iodoform, etc. (See reaction under Chloroform.)

Acetone was manufactured until recently by the destructive distillation of acetate of lime as expressed by the following equation:

$$\begin{matrix} CH_3COO \\ \\ CH_3COO \end{matrix} \!\!\diagdown\!\!\diagup Ca = CH_3COCH_3 + CaCO_3$$

This process while still in use in Europe has been superseded in this country by fermentation of corn primarily, in which acetone and ethyl alcohol are derived as by-products (butyl alcohol being the main product). Considerable quantities of acetone are produced in this way and until quite recently this process was the chief source of supply until a synthetic method was perfected, using propane from natural gas and petroleum.

In the manufacture of chloroform, iodoform, etc., using acetone as a raw material and hypochlorite, the following equation illustrates the reaction that takes place:

$$2\ CH_3COCH_3 + 6CaO.Cl_2 = 2CHCl_3 + Ca(OH)_2 + Ca(C_2H_3O_2)_2 + 3CaCl_2$$

In the case of iodoform, hypoiodite is substituted and the reaction is then similar. An electrolytic method is also in use for the manufacture of these products.

Acetone is also used in the manufacture of sulphanol and in addition to being an excellent solvent for resins and camphors, it is a constituent in many liniments and similar preparations in which it serves as a counter-irritant.

Charcoal has been in use in pharmaceutical preparations since time immemorial. It is recognized as a wonderful gas absorbent, and is employed in tablet manufacture alone and in many combinations.

The wood oils are really by-products, but are fractionally distilled and the fraction boiling between 190° C. and 220° C. furnishes the raw material for the manufacture of U. S. P. creosote and guaiacol and their respective salts that are so prominent in pharmacy.

Pig iron, which is also produced (using charcoal as fuel), would hardly be regarded as a pharmaceutical raw material, but after being processed and refined, it is the source of the iron that enters into the many iron preparations so well known in pharmacy and medicine, a number of which are recognized in the U. S. P.

Perhaps it would not be amiss at this point to describe somewhat in detail the processes involved in the manufacture of the products mentioned above, as comparatively little of an authentic nature has been published regarding the modern hardwood distillation plant, in which many improvements have been made in recent years.

The hardwoods such as beech, birch, maple, oak, hickory, etc., are used exclusively. The wood is cut into lengths or bolts 48 to 52 inches long and then split to answer the following specifications:

not smaller than 3 inches nor larger than 8 inches when measured on either end. Blocked wood (wood cut into small blocks) and waste wood (mill waste, etc.) are also used when obtainable, while some plants, especially in the North, block all the wood where predriers are used to reduce the moisture content prior to distillation.

The wood, after being seasoned (dried) in the open air for nine to twelve months, or treated in predriers at elevated temperatures for 24 to 48 hours, is loaded into steel buggies with slatted sides (to permit ready exit of gases), two and one-half cords to the buggy, and a train of four buggies (10 cords) is pushed into a rectangular steel retort approximately 54 feet long, the doors closed and heat applied from both ends. The modern retort is fired in this manner as against the old so-called single end retort.

Each retort is equipped with two large, copper, tubular condensers, and the distillation is carried on under dual pyrometer control. Heat is applied until the distillation starts, and is continued actively for about three to five hours (according to the moisture content in the wood) to remove the mechanical water, when an exothermic reaction takes place and continues for several hours, during which time external heating is withdrawn. Two series of reactions, primary and secondary, take place in the course of the distillation. The methyl alcohol and acetic acid are among the primary products during the first decomposition of the wood. These primary products react further, yielding secondary compounds, the velocity of the reaction depending on the temperature. Slow distillation produces more secondary reactions because the vapors remain in the retorts longer and undergo a certain amount of polymerization. After the exothermic period is over, regulated firing is again resumed and continued until the volatiles are all driven off and carbonization of the wood is completed. All the condensible products of distillation are collected and constitute the so-called pyroligneous acid or raw liquor, which amounts to 250 to 300 gallons per cord of wood according to the age or seasoning of the wood used. The character of the wood used also has an influence on this figure.

The pyroligneous liquor is a very complex mixture, consisting in the main, of water, acetic acid about 3 to 5 per cent., methyl alcohol 4 to 6 per cent., acetone, and methyl acetate in smaller quantities, numerous aldehydes and ketones of the higher boiling series, small quantities of higher fatty acids, amines, oils, and tars of varying composition.

The liquor is pumped to settling tanks where the so-called insoluble tar is allowed to precipitate, after which the liquor is distilled in double effect long tube vacuum evaporators (Badger type) to remove the tar that is in solution and which is known as soluble or boiled tar. The distilled liquor is allowed to settle and after the removal of wood oils is neutralized with milk of lime to fix the acetic acid as acetate of lime, and again allowed to settle to remove mechanical impurities.

The liquor which is now known as neutral liquor is run through a continuous Lime Lee Fractionating Still consisting of exhausting and concentrating columns; the methyl alcohol, acetone, methyl acetate, etc., are taken from the concentrating column, as crude methanol, at 80 to 90 per cent., while from the exhausting column the acetate liquor is being continuously discharged.

The crude methyl alcohol is then ready for refining which is usually done by a continuous process, using a modern four-column fractionating still of the Barbet type in which chemical treatment for purification is received while the distillation is being carried on. The acetate liquor from the exhausting columns is then run through another double effect vacuum evaporator and concentrated to about 14° Baume, just short of the crystallizing point, after which it is further evaporated on atmospheric drum driers to a heavy sludge and carried on a chain drag to a multipass Huillard drier equipped with a heavy wire, diamond mesh belt, dried continuously, and sacked in burlap bags.

The wood oils are treated separately and distilled for the more valuable fractions containing the phenols and creosotic bodies.

The tars are distilled for the acetic acid and oils they contain and the residual pitch enters the rubber industry as a rubber softener, and is used in insulating material by the insulated wire and cable manufacturers.

The coal mining industry is rather remote from pharmacy, but if we consider for a moment that bituminous coal is the source of coal tar and its many derivatives, from which many products of pharmaceutical importance are derived, the relation is very apparent. In benzol we have the parent product of phenol and the resultant phenolates; salicylic acid and the salicylates, salol, acetanilid, phenacetin, aspirin, etc.

In toluol (toluene), we have the raw material for benzaldehyde (artificial oil of bitter almonds), benzoic acid and saccharin.

Naphthalene has long been known as a raw material in the manufacture of phthalic acid and phthalic anhydride from which phenolphthalein is derived which now enters many pharmaceutical preparations. Naphthalene is also an active antiseptic and insecticide.

Ammonium sulphate recovered in coal tar distillation plants was for many years the raw material for the production of ammonia and ammonium hydroxide (ammonia water), and, of course, the source of the many ammonia salts which are official in the U. S. P., although tremendous quantities of ammonia are now produced by nitrogen fixation.

From the so-called middle oils obtained during the distillation of coal tar, phenol and cresylic acid are derived and these are raw materials for the manufacture of various disinfectants including the well-known Liquor Cresolis Comp., U. S. P.

Coke, the residue of distillation in the carbonization of coal, so well known in metallurgical practice and as domestic fuel, is the chief source of carbonic acid (liquid carbonic acid) used in many reactions for the production of numerous pharmaceutical chemicals, and is used in every drug store where soda fountains are in service, for carbonating beverages, and as a refrigerant. It is also used for carbonating many medicinal waters.

The above resume indicates the dependence and interlocking interests of the pharmaceutical industry especially with the branches of the chemical industry mentioned in this article. During the World War these conditions were emphasized even more strongly. In many instances, as a matter of necessity, and sometimes governmental order, pharmaceuticals were manufactured in chemical plants and many chemicals in pharmaceutical laboratories in order to meet the demand this crisis brought about, not only for our own country, but for those of our Allies who depended on us for many of their pharmaceutical and chemical supplies. Some of these instances came under the writer's observation during this crucial period and cases could be cited from actual experience.

It is very evident that there is, today, a closer bond between pharmacy and chemistry than ever before, and this spirit of harmony has been brought about by the close co-operation existing among research workers both pharmaceutical and chemical.

ADDRESS OF DR. APPEL AT THE FOUNDERS' DAY EXERCISES, FEBRUARY 22, 1930, PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE

THIS IS A SUPERLATIVE age in which we live. The world rolls on more and more rapidly. Life is at all times at high tension. Unrivaled opportunities and unrivaled resources beget unrivaled achievements. Competition and rivalry spur on investigators to a multitude of new discoveries and new ideas in science, in art, in social economics, and even in religion. We are intensely modern. This social condition means much for the common good. Life can be and is made more livable. With the wider sphere of activity there are infinitely greater opportunities for the youth of today than there were for their ancestors. The luxuries of the last century are commonplace necessities now. The world is healthier, and I believe happier and better for the wonderful progress that has been made. But there is another side to the picture. The most wonderful prosperity that the world has ever seen is balanced by comparatively the most utter misery, the greatest abundance with the most absolute want, the most unselfish endeavor and highest altruism by the greatest selfishness. We are superlative in all things.

In addition there are evidences of a canker which, unless controlled may in the future as it has in the past destroy that vitality that has made all these things possible. Complacency and self-satisfaction make the dry rot of progress. We are modern and pride ourselves on being up to the minute, yes up to the second. We boast of the present, contemptuously viewing past conditions. We pride ourselves on being modern, but must not forget that being modern is a relative condition, that England under Elizabeth was very modern, that the Romans, the Greeks, the Egyptians, the Persians, and the Babylonians, and other now forgotten races at the height of their prosperity considered themselves very modern. In their writings will be found the same satisfaction expressed over the wonderful advances they had made in knowledge and civilization that we see today, and the same feeling of half pity, half contempt for those others present and past who have no place in the sun. They reflect the same self-complacency and self-satisfaction which to a degree characterizes our own age, undoubtedly this spirit tends to the exaggerated ego both national and individual and is a real danger signal.

To counteract this potential menace it is necessary for society as a whole to cultivate the humble mind and spirit of the real scientist, sage or philosopher who from his knowledge has the true perspective of fact and recognizes the relativity of the times. We must sit before the shrine of history and learn to appreciate the true meaning of this progress of the human race, that it is an orderly evolution, that the macrocosm is greater than the microcosm, that our age with all its glory is but an incident in a grand scheme of development, that relatively with our advantages we are no greater in our accomplishments than civilizations of the past which we now term barbaric, and that without question future generations will view our "miracles" as commonplace, and our civilizations and refinements as crude. Old Chaucer, five hundred and more years ago, wrote:

"For out of the old fieldes, as men seath,
Cometh all this new corne from yere to yere,
And out of old bookes in good faithe
Cometh all this new science that men lere."

So that for the good of our souls, in the prevention of an overdevelopment of that feeling of self-complacency that is so pleasant, it is advisable for us in our busy life to pause for the moment and set aside an hour or a day like unto this one, on which we can look backward over the age-long history of the race and with a humble mind make real comparison with that gone before to the end that we may properly evaluate ourselves and our accomplishments and we may be able to discern when we discount our greater aids and opportunities, that the so wonderful advances and achievements of today, epoch-making as we view them, are really comparatively no more wonderful than the work of the philosophers and scientists of other ages, but form simply an incident in the orderly evolution of a great plan and that they are the direct outcome of labor and thought of men now almost forgotten—

"For out of old bookes in good faithe
Cometh all this new science that men lere."

In fair comparison with existing social conditions and a true appreciation of relativity, the discoveries of Edison, Koch and Lister, the achievements of Ford and our great industrial leaders are no more wonderful than was the knowledge of the priests of Osiris, or the trading adventures of the Phœnicians when they too were modern.

We celebrate this Founders' Day, not only to glorify the deeds of the sixty-eight founders of this institution, but also to give us an opportunity to make an unprejudiced survey of our present state with all humbleness of spirit and appreciation of our present blessings.

You have here today in this magnificent institution with its well-equipped laboratories, its superb equipment, its learned faculty, a College of Pharmacy and Science, the oldest in the country and one which exemplifies the true ideals of the art and science it teaches. It is a far cry from this occasion and the environments of this celebration to the meeting of your professional ancestors in Carpenters' Hall one hundred and nine years ago. Your founders could never have visioned the result of their labors. But the spirit of independence, of determination to raise professional standards and to elevate the profession of Pharmacy has continued through the century to direct the destinies of this College. You have at your disposal knowledge of fields of professional application undreamt of then, but to a critical mind our methods of utilizing our knowledge of bacterial life for the purpose of prevention and cure of disease is no more wonderful than the isolation of the first alkaloid, the introduction to England of croton oil, or the extraction of iodine from sea water were in 1821 when these discoveries with many others were announced.

But it is not my purpose to trace in detail the growth and history of this institution, but to consider for a short time the general profession of Pharmacy and its relation to society at large as represented by the field of public health. In the first place, let it be understood that Pharmacy is a profession, not a trade, that it is both a science and an art, not a craft, that it has a broad field and plays a necessary part in our social fabric. Like medicine it is as old as the human race. From the common ancestor—the priestcraft of Egypt—it grew and flourished until when the barbarians overran the ancient world and destroyed the ancient civilizations for a time both professions went into eclipse. But the destruction of the Alexandrian library did not completely obliterate the work of the Arabian and Egyptian physicians. By slow and arduous steps the heights were regained and while medicine sprang from the barber shop of France, pharmacy likewise divorced herself from the grocery store and hardware shop. It seems to me that while medicine involves the thorough study of the causes, symptoms, treatment, and prevention of disease, pharmacy has to do with the careful study, manufacture, compounding and preparing of the necessary remedies to be used in that treatment and prevention.

Like all other professions, it has its departments or specialities. It embraces the entire field from the procuring or production of the raw materials to the retailing of them to the customer. It involves research of the most painstaking kind. It calls for proper standardization and protection from adulteration of the drugs or other materials used. Pharmacy as a profession must always be on guard.

And what is Public Health? It is the practical application of the truths of prevention. It involves not only the prevention of specific contagious disease through isolation, quarantine, or the development of immunity by the use of various medicinal agents, but also through propaganda and education of the public the observance of the right laws of living that society as a whole and as individuals may attain and retain health. It means the creation of a civic conscience on the part of municipalities and a personal appreciation on the part of citizens that they have certain sanitary duties towards their neighbors. It means the attainment of pure water, pure food, pure milk, proper sewage and industrial waste disposal, proper housing conditions, proper sanitary surroundings in workshop and factory, proper personal habits in regard to eating, sleeping, clothing, rest and play. It means the oversight of the children that they may attain adult life with the minimum of handicaps. It means the proper general knowledge of the importance of care of the expectant mother that her babe may be born with its proper birthright. It means all these things to the end that the individual may live out his natural span of life with the least amount of wear and tear, that the accidental infections may be banished and that the menace of the degenerative diseases of middle life may be lessened or at least postponed. The health of a community is its most valuable asset and it can be obtained not by a series of laws, thou shalt and thou shalt not, but only by an educated public opinion and a voluntary observance on the part of municipality and individual of the few simple natural laws whose observance is necessary to attain the goal.

Like pharmacy and curative medicine, preventive medicine or public health is almost cœval with history. While accurate knowledge of cause and effect was denied the ancients, observation showed the present menace and even with faulty deductions preventive measures were common. It is a far cry from a modern well-sewered city with proper water system to the wandering tribe of the gray dawn of history, but in both cases the truth was recognized that always in life are the seeds of death. Continuous residence of a tribe in one locality

inevitably brought disease, and the tribes became nomadic. It makes no difference whether the cause was ascribed to demons or devils or an angry diety or to the presence of the bacillus of typhoid, the end result was the same and comparatively speaking the witch doctors or wise men of the primitive tribe grasped a remedy as important to that age and state of society as was the demonstration of the cause of the Plymouth epidemic to our own age. It is a far cry from the amulet of the witch doctor or the camphor ball of the days of the bubonic plague or the yellow fever scourge to the package of preventive toxin-antitoxin, but they were all the results of incessant search for a means of protection against a recognized danger. The Mosaic Law was as important a public health treatise as the latest contribution of the national Public Health Service. Wonderful advances have been made in the field of public health. The expectation of life of a new-born babe has been increased from the sixteen years of not many centuries ago and the forty-nine years of 1900 to almost sixty years today. The horrors of the great scourge epidemics are things of the past. The advances in this particular field have been marvelous in the last fifty years as the result of the birth of the new science of bacteriology, but again in our pride we must remember that even these discoveries had been impossible but for the accumulation of the store of observations made in times past, gradually recognizing an effect and groping mistakenly into the unknown to determine the cause and remedy.

Let me for a moment trace the part pharmacy as an art and a science has to play in this great altruistic fight for social health. A part is self-evident. From investigators in laboratory and in clinic comes the discovery of the cause of a given disease and the suggestion of a remedy or a means of prevention. In the pharmaceutical laboratory that remedy is made available for practical use, standardized and kept safe. In this manner has come into being the long line of biological products invaluable both in curative and preventive medicine. Insulin was found to be of value in the treatment and control of diabetes but the manufacturing pharmacist made it available for practical use. The ingestion of liver is necessary to prevent the ravages of pernicious anæmia and again the laboratories of pharmacy produced extracts increasing the power of control. In France among our troops and on the Mexican border typhoid was practically unknown, for in addition to the care of the sanitary engineer, these same laboratories supplied the government with a reliable preventive vaccine. The

universal use of toxin-antitoxin to the young and susceptible child will eventually eliminate diphtheria as smallpox has been practically eliminated, at least in Pennsylvania by the universal use of vaccine virus.

These achievements are all of admitted importance to Public Health, but to my mind the retail pharmacist if he be a true student of his profession has the greatest opportunity. He is continuously in contact with the public, and his opportunity by advice to aid in the education of the public is unlimited. True to do this he must be a real student and must be familiar with his wares. The local drug store which prospers solely by the sale of patent or proprietary medicine of which the druggist knows nothing save the price and the testimonial printed on the label is as pernicious as the physician who practices from the satchel of the enterprising detail man and prescribes pills or lotions, of the ingredients of which he knows nothing, purchasing his remedies cheaply regardless of standards. Such men are found in all professions and constitute a reproach and a menace, but the presence of the unworthy does not change the ideals of the profession. The retail pharmacist to fulfil his mission must be a student and a scientist. He must be a psychologist as well as a physiologist, a chemist as well as a dispenser. He must have a comprehensive knowledge not only of his remedies but also of the diseases for which they are indicated and with this knowledge in a hundred ways he can legitimately and ethically do his part for public health. Your President, himself, when Director of Public Health, has repeatedly borne witness to the yeoman assistance given by the pharmacists of Philadelphia during the stress of the terrible epidemic of influenza in 1918. To my mind the retail druggist stands as the guardian of the purity of his wares, as a possible protector of the public against assaults of predatory quacks and faddists.

And going further, the pharmacist is a member of a profession of high ideals and great possibilities. Each individual owes a certain debt to society as a whole and it seems to me in view of the ideals of his profession and his own knowledge, that the pharmacist is well equipped to take his stand in the line of battle for general public health and do his part in molding public opinion along proper lines. In this way he renders to society the debt he owes it.

And to this College of Pharmacy and Science, the oldest in the country, with its wonderful equipment and high ideals, is due the credit for a great part of the work of placing pharmacy in America

on an enduring foundation. The dreams of the founders have been more than materialized. Its history of progress and achievement of more than a hundred years shows a high and honorable record. Its educational influence is nation wide. But we cannot be too self-complacent; we are not at the end of the trail. The very progress of which we are all so proud cannot satisfy us but should rather urge us on to greater endeavor.

PRESERVATION OF FATS*

By George W. Fiero†

FATS AND FIXED oils not only are essential from the standpoint of a dietitian but also play an important part in many industries. Jamieson [1] states that the life and progress of a nation depend in no small measure upon its supply of fats and fatty oils. The requirements for them continually increase as the population grows and industries expand. Most animal and vegetable fats and fatty oils, however, are more or less susceptible to rancidity. The *New World Dictionary* defines the term "rancid" as "having a rank, unpleasant smell." This change in the fat upon aging also results in chemical changes which may render the substance unfit for use in commerce as well as render it useless for human consumption. The rancidity problem is a very serious one to the soap manufacturer as many soaps become dark colored when rancid. Pharmaceutically, rancid ointments not only have a very disagreeable odor but also possess certain irritant properties which render them unfit for medicinal use.

The Chemistry of Rancidity. Although the literature contains many published observations, the exact nature of rancidity is unknown. There are certain factors, however, which seem to be definitely related to the problem. The most important substance necessary for rancidity is oxygen. Rancid fats contain oxidation products which may easily be detected in the laboratory. Rancid fats exhibit peroxide properties as indicated by two tests: (1) If a rancid fat is shaken with solution of potassium iodide, the iodine is liberated.

*Part of a thesis presented to the University of Southern California, Los Angeles, in partial fulfillment of the degree of Master of Science.

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This may easily be detected by means of starch test solution which develops a blue color. Often the amount of iodine liberated is sufficient to give the solution an amber color. (2) If a rancid fat is shaken with hemoglobin, sodium chloride solution, and alcoholic solution of guaiac, a blue color is developed which is similar to that given by hydrogen peroxide under the same conditions. Rancid fats contain aldehydes and respond to the standard aldehyde tests. The Kreis Test for rancidity which was used in this experiment and is the standard test used by the Department of Agriculture is said to be due to certain higher aldehydes and ketones.[2] Not only do rancid fats contain definite oxidation products, but it has been found that rancidity will not develop in absence of oxygen.[3]

Moisture is a very imprtant factor in the problem. Rancid fats usually have an abnormally high acid value; in fact, some claim that acid fats are rancid and rancid fats are always acid. It has been pointed out that acidity usually precedes rancidity.[4] This primary acidity is no doubt due to the hydrolysis of the fatty ester by the moisture present. Many authorities believe that moisure is essential to this deterioration and that rancidity will not develop in fats which are absolutely free from water.

There are other factors which, although probably not essential, have a definite influence upon the rate of development. Rancidity develops but slowly in the dark.[5] This was verified by placing samples of lard in earthen wide-mouth ointment jars in a light place at a temperature of 20° C. and at the same time placing similar samples in a dark place at the same temperature. Rancidity developed in the first samples in three to four days while the second samples required fifteen to sixteen days. Heat also hastens this chemical action; similar samples placed in sunlight at 35° C. developed rancidity in two days. Metals have also been found to have an effect upon rancidity.[6] This was verified by placing samples of lard in metallic containers; these samples developed rancidity in ten days while lard in the same size earthen containers under the same conditions required sixteen days.

The action of micro-organisms in rancidity seems to be a question. The literature indicates that many believe that they are a factor. An enzyme has been discovered which is thought to cause rancidity and hence named "Rancidase."[7] Other workers have found that rancidity will develop in fats which are free from micro-organisms.[8]

In order to ascertain the effect of micro-organisms upon the development of rancidity in lard, ten samples of lard, stoppered with cotton plugs, were sterilized in an autoclave at 20 pounds for a period of twenty minutes. The samples were allowed to stand for ten weeks together with unsterilized samples. The sterile samples did not develop rancidity in this time while the unsterile samples became decidedly rancid.

Pure saturated fats will not develop rancidity, according to Jamieson.[9] On the other hand, it is usually noticed that unsaturated fats are very susceptible to rancidity and that the rate of development is more or less proportional to the iodine number of the fat which is an indication of the extent of unsaturation. One author [10] explains rancidity as the action of the oxygen attacking the "double bond" forming a peroxide which later breaks up forming aldehydes and ketones of lower molecular weight. The glyceryl portion of the fat molecule is also oxidized to ketones and aldehydes. Various other theories have been advanced, but most of them deal with the oxidation of the unsaturated portion of the fat.

The Action of Preservatives. There are several hypotheses explaining the action of preservatives on fats. Many authors claim that the preservative acts as a "negative catalyst upon the oxidation" of the fat. Holm and Greenbank [11] believe that the action of preservatives is due to the presence of the "OH" radical in the molecule. They point out such substances as dihydrostearic acid, glycerin, resorcinol, phenol, various alcohols, etc., as being good preservatives because of the "OH" groups in their structures. They also note that castor oil is less susceptible to rancidity than other oils with a similar high iodine value and claim this to be due to the "OH" groups in the ricinoleic acid molecule. Smith and Wood [12] disprove the catalytic hypothesis in their work which indicates that preservatives retard the development of rancidity or oxidation for a short time (which varies with the individual preservative) after which oxidation takes place at the normal rate. This would indicate that the action of the preservative is to prevent oxidation of the fat by themselves becoming oxidized. After they are fully oxidized, they would have no preserving action. Many unsaturated substances and reducing agents have been reported as good preservatives. The development of rancidity in all fats may not be identical as is indicated by the fact that methods of renovating rancid coconut oil do not renovate rancid lard.[13]

Historical Review—Preservatives. The most common preservative for pharmaceutical fats is benzoin. It has been pointed out [14] that the preservative action is due to the benzoic or cinnamic acid content, but Husa [15] found that as much as four per cent. of benzoic or cinnamic acid would not preserve lard. Even benzoin, itself, is far from a perfect preservative. A sample of benzoinated lard in sunlight at 33° C. developed rancidity in three days. Samples of benzoinated lard or ointments prepared from this compound are commonly found rancid in drug stores. Balm of gilead buds has also been used as a preservative, but imparts to the fat a distinct color.[16]

The following substances have been reported as very good preservatives for fats and oils: sodium thiosulphate or a mixture of sodium thiosulphate with sodium bicarbonate,[17] thymol, stannous chloride, sodium silicate, acetaldehyde anilin condensate, agerite,[18] sulphides of antimony, zinc, arsenic and lead,[19] pyrogallic acid,[20] hydroquinone,[21] betanaphthol,[22] alphanaphthol,[23] salicylic acid,[22] and urea or basic organic nitrogen compounds.[24]

Experimental Procedure. Various substances were mixed with pure, fresh leaf lard and allowed to stand in unstoppered test-tubes to ascertain the preservative action. At least six different percentages of each substance were prepared to determine the minimum quantity which would preserve the fat. Each group of twelve samples contained two samples of untreated lard used as "controls." Some samples were kept in a warm, light room while others were placed in a cooler, darker room. Those in the light room developed rancidity more quickly; untreated lard kept four weeks in the light room had the same intensity of rancidity as that in the darker room for ten weeks. Also eight weeks in the light room were equivalent to twenty-five weeks in the dark room.

The "control" samples were tested for rancidity weekly and the entire lot twice: first after four weeks in the light room or ten weeks in the dark room and second after eight weeks in the light room or twenty-five weeks in the dark room. The intensity of rancidity was determined by the Kreis Test:

> Five cc. of the molten fat are shaken with 5 cc. of concentrated hydrochloric acid. The addition of 5 cc. of 0.1 per cent. ethereal solution of phloroglucinol produces a pink to red color, the extent of rancidity being indicated by the intensity of the color.

Some substances, such as oil of clove, contain aldehydes or ketones which interfere with the test and in these samples rancidity must be detected by the odor and taste. In all cases the Kreis Test was verified by the odor or taste. The following table indicates the results:

THE EFFECT OF PRESERVATIVES UPON RANCIDITY IN LARD

KEY

\+ indicates definitely rancid
= indicates but slightly rancid
— indicates free from rancidity

Preservative	Per cent.	Kreis Tests	
Calcium Hydroxide	0.12—2.00	+	+
Terebene	0.12—2.00	+	+
Benzyl Benzoate	0.12—2.00	+	+
Sodium Benzoate	0.06—0.50	+	+
Sodium Benzoate	1.00—2.00	—	=
Sodium Benzoate*	0.05—0.08	=	+
Sodium Benzoate	0.10—0.40	—	+
Sodium Benzoate	0.60—2.50	—	=
Sodium Thiosulphate	0.12—2.00	+	+
Salicylic Acid	0.12—2.00	+	+
Acetysalicylic Acid	0.12—2.00	+	+
Menthol	0.12—2.00	+	+
Vanillin	0.06—1.00	+	+
Coumarin	0.06—1.00	+	+
Antipyrine	0.06—1.00	+	+
Acetphenetidin	0.12—2.00	+	+
Acetanilid	0.12—2.00	+	+
Acetaldehyde	0.06—1.00	+	+
Acetaldehyde	2.00—2.50	=	+
Cloretone	0.06—1.00	+	+
Resorcinol	0.12—0.50	—	=
Resorcinol	1.00—2.00	—	—
Phenol	0.12—2.00	+	+
Methenamine‡	0.06—2.50	—	—
Safrol	0.03—0.25	+	+
Safrol	0.50—1.00	—	+
Oil of Sassafras	0.12—0.50	+	+
Oil of Sassafras	1.00—2.00	=	=
Oil of Pine Needles	0.12—2.00	+	+
Oil of Organum	0.06—2.00	+	+
Oil of Cinnamon	0.12—2.00	+	+
Oil of Eucalyptus	0.12—2.00	+	+
Oil of Rosemary	0.20—3.00	+	+

*The sodium benzoate was dissolved in water, neutral soap added and emulsified with the molten lard.

‡The lard with methenamine became yellow colored on standing.

†Oil of clove interferes with Kreis Test; rancidity detected only by odor and taste.

Mixture	Per cent.	Kreis Tests	
Oil of Clove†	0.38—3.00	—	—
Guaiacol Carbonate	0.12—2.00	+	+
Guaiacol	0.01—0.02	+	+
Guaiacol	0.03—0.04	—	+
Guaiacol	0.06—1.50	—	—
Thymol	0.05—0.15	+	+
Thymol	0.30—1.60	—	+
Thymol	2.50—3.00	—	—
Creosote	0.06—0.12	—	+
Creosote	0.25—2.00	—	—

DEVELOPMENT OF RANCIDITY IN MIXED FATS

Mixture	Per cent.	Kreis Tests	
Stearic Acid Lard	0.4—50.0 q. s.	+	+
Hydrogenated Oil Lard	0.4—12.5 q. s.	—	+
Hydrogenated Oil Lard	25.0—50.0 q. s.	—	—
Paraffin Lard	0.4—50.0 q. s.	+	+
White Wax Lard	0.4—50.0 q. s.	+	+
Yellow Wax Lard	0.4—50.0 q. s.	+	+
White Petrolatum Lard	0.4—25.0 q. s.	+	+
White Petrolatum Lard	50. 50.	—	+
Wool Fat Lard	0.4—50.0 q. s.	+	+
White Wax Petrolatum Lard	25.0 25.0 50.0	—	—
White Wax Petrolatum Lard	12.5 12.5 50.0	—	+
White Wax Petrolatum Lard	0.4—6.2 0.4—6.2 q. s.	+	+
Liquid Petrolatum White Wax Lard	6.2—25.0 6.2—25.0 q. s.	—	—
Liquid Petrolatum White Wax Lard	0.4—3.1 0.4—3.1 q. s.	+	+

Mixture	Per cent.	Kreis Tests	
Liquid Petrolatum	25.0		
Petrolatum	25.0	+	+
Stearic Acid	25.0		
Lard	25.0		
Liquid Petrolatum	25.0		
Petrolatum	25.0—50.0	—	+
Lard	q. s.		
Liquid Petrolatum	25.0		
Stearic Acid	25.0—50.0	+	+
Lard	q. s.		
Liquid Petrolatum	25.0		
White Wax	25.0	—	—
Lard	50.0		
Liquid Petrolatum	25.0		
Paraffin	25.0—50.0	—	—
Lard	q. s.		
Liquid Petrolatum	25.0	+	+
Lard	75.0		
Stearic Acid	25.0		
Petrolatum	25.0—50.0	+	+
Lard	q. s.		
Petrolatum	10.0		
Stearic Acid	10.0	+	+
Paraffin	15.0		
Lard	65.0		
Petrolatum	50.0		
Wool Fat	25.0	+	+
Lard	25.0		
Petrolatum	25.0		
Wool Fat	50.0	—	+
Lard	25.0		
Paraffin	25.0		
Wool Fat	25.0—50.0	+	+
Lard	q. s.		
Petrolatum	25.0		
Wool Fat	25.0	—	+
Paraffin	25.0		
Lard	25.0		

The following ointment bases did not develop rancidity after ten weeks in a warm, light room or twenty-five weeks in a cool, dark room:

White Wax, Yellow Wax, Paraffin, Wool Fat, Hydrous Wool Fat, White Petrolatum, Yellow Petrolatum, Liquid Petrolatum, Hydrogenated Oil, or any mixtures of the above fats.

Summary. Of the large number of preservatives used, only a few were found to have preservative effects. Those which completely preserved the lard were:

Resorcinol, one per cent.
Oil of Clove, 0.38 per cent.
Guaiacol, 0.06 per cent.
Thymol, 2.5 per cent.
Creosote, 0.25 per cent.

Some substances showed some preservative effect, the lard remaining free from rancidity for four weeks in a warm, light room or ten weeks in a cool, dark room, but did not prevent rancidity from developing in eight weeks or twenty-five weeks respectively.

Safrol, 0.5 per cent.
Sodium Benzoate, 1 per cent.
Sodium Benzoate (dissolved in water and emulsified with the fat by means of neutral soap), 0.1 per cent.
Methenamine completely prevented rancidity, but developed a yellow color on standing.

Most mixtures of lard with other fats developed rancidity. Lard with the following did not develop rancidity:

Hydrogenated Oil, 25 per cent.; White Wax and Petrolatum, 25 per cent. of each; White Wax and Liquid Petrolatum, 25 per cent. of each; Paraffin and Liquid Petrolatum, 25 per cent. of each.

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THE RELATION OF MEDIA pH TO THE BACTERIOSTATIC ACTION OF DYES

By S. E. Owen

SOME OF THE PRESENT aniline dyes have been found to have a demonstrable power to inhibit the growth of bacteria. A well known instance of this peculiar chemical selectivity is that of gentian violet toward Gram positive organisms.[1] It is generally true that dyes of the triphenyl-methane type may inhibit the growth of Gram positive organisms.[2] There are some exceptions to this action but this is not surprising when one considers the fact that some bacteria are "Gram amphophiles."

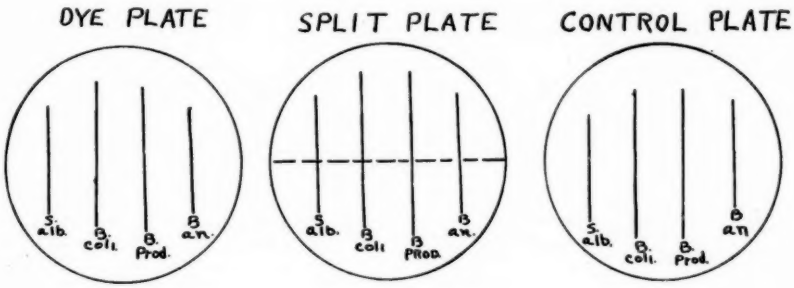
The complex phenomena of bacterial staining has not been completely explained either by the physical or by the chemical theories. Recent work seems to emphasize the chemical viewpoint in the explanation of bacterial stains. Bacteria resemble proteins in retaining acid dyes when in acid solution and basic dyes when in basic solutions. One would expect then to find an iso-electric range where there would be little if any stain retained by the bacteria. Such an iso-electric range has been located by Stearns and Stearns[3] at about pH 2-3. While it is true that this range is too highly acid to permit many bacteria to grow, we must admit that hydrogen ion concentration may have some influence on the bacteriostatic action of dyes. Perhaps as Dubois[4] suggests, the dye may owe its inhibitory powers to the fact that the media is poised at an oxidation potential outside the range in which inhibited organisms can grow. Churchman,[5] however, has shown that the bacteriostatic action of gentian violet is not significantly affected by a change in pH of media.

We have found in our laboratories that bacteria do not retain the food dyes as stains. Nor can we produce fast stains with these

dyes by a moderate concentration of acid or alkali. The experimental work on which this report is based includes ten of the certified food dyes, gentian violet, methylene blue and basic fuchsin.

Experimental

Agar with a pH range from 4.4 to 10.4 was prepared and the dye added to the media directly before pouring the plate. The concentration of the food dyes used in these plates was 1:6000, of gentian violet 1:120,000, of methylene blue 1:12,000, and of basic fuchsin 1:24,000. The test organisms used were staphylococcus albus, B coli communis, B. prodigiosus and B. anthracis. Broth cultures of these were used as a transplant source. Each plate made had a control plate which contained no dye but whose pH corresponded to that of the dye plate. This separate control plate was found more suitable than the split plate as used by Churchman.[5] Each test was run in duplicate. Plates showing no first growth were again streaked with the organism that failed to grow the first time. Broth was also tried as a media, but as the results were concordant with those obtained on agar, the latter media was used because of convenience. NaOH was used to obtain the pHs in the alkaline range and for the acid media HCl was employed. If the alkaline range was extended above 10.4 a buffer mixture was found advisable.



To be certain that our twenty-four-hour incubation period or the bacterial growths themselves did not change the pH of the media, blanks were prepared, incubated and the pH determined. The pH of these growth plates and blank plates were found to check within experimental error. The sketch shows the arrangement of the plates and the placing of the streaks. The table shows the results. A positive sign indicates growth, a negative sign no growth.

TABLE OF RESULTS

pH	Organisms	Methylene blue	Gentian violet	Basic fuchsin	Control	Indigo	Guinea green	Light green S. F. yellowish	Tartrazine	Orange 1	Ponceau 56	Amaranth	Fast green F. C. F.	Erythrosine	Naphthol yellow
4.4	S. al	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	B. co	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	B. pr	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	B. an	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5.4	S. al	—	—	—	#	#	#	#	#	#	#	#	#	—	#
	B. co	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. pr	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. an	—	—	—	#	#	—	#	#	#	#	#	#	—	#
6.4	S. al	—	—	—	#	#	#	#	#	#	#	#	#	#	#
	B. co	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. pr	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. an	—	—	—	#	#	—	#	#	#	#	#	#	—	#
7.4	S. al	#	—	—	#	#	#	#	#	#	#	#	#	#	#
	B. co	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. pr	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. an	—	—	—	#	#	—	#	#	#	#	#	#	—	#
8.4	S. al	—	—	—	#	#	#	#	#	#	#	#	#	#	#
	B. co	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. pr	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. an	—	—	—	#	#	#	#	#	#	#	#	#	—	#
9.4	S. al	—	—	—	#	#	#	#	#	#	#	#	#	#	#
	B. co	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. pr	#	#	#	#	#	#	#	#	#	#	#	#	#	#
	B. an	—	—	—	#	#	#	#	#	#	#	#	#	—	#
10.4	S. al	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	B. co	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	B. pr	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	B. an.	—	?	—	—	—	—	—	—	—	—	—	—	—	—

Interpretation of Results

In the acid range at pH 5.4, selective action, on the Gram positive organisms, of basic fuchsin, methylene blue and gentian violet is parallel. Staphylococcus grew on the methylene blue plate at pH 7.4. At pH 4.4 there was no growth of the test organisms on these plates. In the alkaline plates selective action of these dyes at pH

9.4 is evident. Beyond pH 9.4 the same dyes were disrupted and B. anthracis grew. At pH 12.4 (not charted) there was no growth of the organisms.

Eight of the food dyes tested indicated no bacteriostatic action at pH 4.4 to 9.4. Erythrosine, which is a sodium or potassium salt of tetra iodoflourescein, apparently inhibits the growth of B. anthracis at all pHs studied. On the acid side and at pH 7.4 guinea green, a triphenyl-methane dye, inhibits the growth of B. anthracis.

Summary

1. The pH value of media is an insignificant factor in the selective action of gentian violet, basic fuchsin and perhaps also methylene blue.

2. Eight of the certified food dyes tested show no bacteriostatic action at pHs ranging from 5.4 to 10.4.

3. Guinea green inhibits the growth of B. anthracis in the acid range and at pH 7.4 but not in other alkaline pHs greater than this.

4. Erythrosine inhibits the growth of B. anthracis at all pHs studied.

5. The work on dyes and the preparation of non-toxic germicides will be continued and a later report will give further results.

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SOLUTION OF ARSENOUS AND MERCURIC IODIDE*

By Morris G. Acton, Jr., Ph. G.

THE OBJECT of this thesis is an analytical investigation into the chemistry of "Solution of Arsenous and Mercuric Iodide," including the assay and stability.

The U. S. P. X. recognizes under the title of "Liquor Arseni et Hydrargyri Iodidi," or "Solution of Arsenous and Mercuric Iodide," commonly called Donovan's Solution, an aqueous solution containing not less than 0.95 per cent., nor more than 1.05 per cent. AsI_3; and not less than 0.95 per cent., nor more than 1.05 per cent. HgI_2.

Various workers have found that this solution undergoes change on keeping.

(1) W. H. Schulze states that the AsI_3 undergoes a rapid change upon standing which appears to be very much accelerated by exposure to light. He proposes that the assay for AsI_3 be changed to an assay for total arsenic due to the fact the present method for determining the AsI_3 is unreliable.

(2) In a subsequent article he states the solution undergoes a rapid change due to the oxidation of the trivalent to the pentavalent arsenic which is accelerated by exposure to light. The change in color of the solution is due to the liberation of iodine which takes place when the arsenous compound has been completely oxidized.

(3) J. Rosin stresses the oxidation of the trivalent arsenic to the pentavalent form and found at the end of one year and eleven months a loss of over one-half of the AsI_3 content, although the total arsenic remained the same.

(4) H. A. Langenhan states that the cause of the change in color of the solution is not clearly understood, one writer claiming that the colored solution did not give a positive test for free iodine with starch test solution.

The U. S. P. X. Assay:

A. For AsI_3.

Measure exactly 25 cc. of Solution of Arsenous and Mercuric Iodide into a flask. Dilute with 25 cc. distilled

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water, then dissolve 2 Gm. $NaHCO_3$ in this solution and titrate with N/10 I. V. S. using starch test solution as indicator. Each cc. N/10 I. V. S. corresponds to 0.02279 Gm. AsI_3.

There is no difficulty encountered with this assay if followed as outlined and accurate results are insured.

B. For HgI_2.

Measure exactly 25 cc. of Solution of Arsenous and Mercuric Iodide into a flask, add 5 cc. of KOH T. S. and 5 cc. of HCHO T. S. and warm the mixture on a water bath until the mercuric salt has been completely reduced to metallic mercury. Carefully decant the clear supernatant liquid from the residue of metallic mercury and wash the mercury carefully by decantation with two successive portions of 25 cc. each of distilled water. Dissolve the residue of metallic mercury in 5 cc. of HNO_3 by the application of gentle heat, dilute the solution with 50 cc. distilled water, add 2 cc. of ferric ammonium sulphate T. S. and titrate with N/10 KCNS. Each cc. of N/10 KCNS corresponds to 0.02272 Gm. of HgI_2.

In this assay the metallic mercury resulting from the reduction of the mercuric salt in alkaline solution is very finely subdivided and some of these finely divided particles float on the surface of the liquid instead of settling to the bottom of the flask. These floating particles of mercury are lost if the supernatant liquid is decanted.

It was found by pouring the supernatant liquid through a filter that this loss of mercury could be avoided. The mercury was dissolved from the filter by means of a small amount of HNO_3, and the resultant solution added to the residue of metallic mercury dissolved in HNO_3 and the entire solution then titrated with N/10 KCNS.

A U. S. P. X. preparation assayed in duplicate by this method yielded results of 0.973 per cent. AsI_3 and 0.988 per cent. AsI_3.

Still another method of assay for HgI_2 was tried as follows:

Measure exactly 25 cc. of Solution of Arsenous and Mercuric Iodide into a glass-stoppered bottle, add 10 cc. NaOH (10 per cent.) and 10 cc. HCHO (36 per cent.) and warm on a water bath until the mercuric salt has been completely

reduced. Add 25 cc. concentrated HCL and an excess of N/10 I. V. S. Shake the mixture until all the reduced mercury has been dissolved, being sure to have an excess of N/10 I. V. S. present. Titrate the excess of N/10 I. V. S. with N/10 $Na_2S_2O_3.5H_2O$ V. S., using $CHCL_3$ as indicator. Carry out a blank, using identical portions of reagents.

This method is somewhat long and does not yield such good results.

Stability:

It is a fact recognized by the profession and shown by previous workers upon the subject that fresh samples of a Solution of Arsenous and Mercuric Iodide deteriorate rapidly upon keeping and as stated by Schulze this deterioration is very much accelerated by exposure to light.

A solution prepared on February 16, 1927, was stored under four different conditions and showed the following percentages of AsI_3 on the stated dates.

	Protected from Sunlight		Exposed to Sunlight	
Date	Amber Glass	Clear Glass	Amber Glass	Clear Glass
Feb. 16	0.987	0.987	0.987	0.979
Feb. 17	0.979	0.979	0.987	0.970
Feb. 18	0.970	0.970	0.970	0.965
Feb. 19	0.970	0.970	0.970	0.961
Feb. 21	0.961	0.961	0.961	0.952
Feb. 23	0.952	0.952	0.952	0.943
Feb. 25	0.943	0.943	0.943	0.934
Mar. 2	0.924	0.924	0.924	0.904
Mar. 9	0.886	0.886	0.886	0.875
Mar. 16	0.843	0.838	0.843	0.832
Mar. 30	0.769	0.769	0.779	0.750
Apr. 13	0.692	0.673	0.688	0.649
Apr. 27	0.606	0.591	0.606	0.548
May 16	0.461	0.442	0.457	0.389

It is concluded from the comparison of the results of these experiments that there is not a sufficient difference in the rates of deterioration to warrant any unusual care in the storage of this solution.

Another factor heretofore not mentioned and of noteworthy importance is the increased acidity of older solutions.

Experiments with freshly prepared aqueous solutions of AsI_3 showed an acid reaction which can be measured with N/10 NaOH V. S., using methyl orange as indicator. This acidity is explainable by the probable hydrolysis of the AsI_3.

$$AsI_3 + 3H_2O = H_3AsO_3 + 3HI$$

Of these products only HI is measured with methyl orange indicator. As the trivalent arsenic is oxidized to the pentavalent condition there is produced H_3AsO_4 which toward methyl orange acts as a monobasic acid and explains the increased acidity of older solutions.

A solution prepared on March 2, 1927, was assayed every week over a period of eleven weeks for (1) the AsI_3 content by use of I. V. S., and (2) for acidity calculated to AsI_3 by use of NaOH V. S. and methyl orange indicator. The difference between these two results in column (3) represents the AsI_3 oxidized to the pentavalent condition.

Date	% AsI_3 by titration with I. V. S.	% AsI_3 by titration with NaOH V. S. with M. O. indicator.	% AsI_3 oxidized to pentavalent condition
Mar. 2	0.950	0.945	0.004
Mar. 9	0.923	0.946	0.023
Mar. 16	0.886	0.979	0.093
Mar. 23	0.846	0.996	0.149
Mar. 30	0.822	1.011	0.189
Apr. 6	0.789	1.011	0.222
Apr. 13	0.741	1.028	0.287
Apr. 20	0.712	1.044	0.332
Apr. 27	0.668	1.060	0.392
May 4	0.606	1.077	0.471
May 11	0.558	1.085	0.527

By comparison of these results a gradual increase in acidity will be seen to accompany the decrease in per cent. of AsI_3.

The determination of the pentavalent arsenic produced in the aging of the solution was made as follows:

> Pipette accurately 10 cc. of Solution of Arsenous and Mercuric Iodide into a glass-stoppered bottle and add 10 cc. of KI (5%) and 20 cc. concentrated HCL. Titrate the liberated iodine with N/10 $Na_2S_2O_3.5H_2O$ V. S., using $CHCL_3$ as indicator. Calculate results to % AsI_3.

This percentage of pentavalent arsenic was found to increase with the decrease in percentage of AsI_3 which indicates oxidation on the part of the trivalent arsenic.

When the pentavalent arsenic is calculated in terms of AsI_3 and added to the per cent. of AsI_3 actually present at the time of the pentavalent arsenic determination, the sum of the two per cents. gives the total arsenic content calculated to AsI_3 and closely corresponds to the original per cent. of AsI_3 or 0.950% AsI_3 present in the solution made on March 2, 1927.

Date	% AsI_3 actually present	% pentavalent arsenic calculated to AsI_3.	Total arsenic calculated to % AsI_3.
April 27	0.668	0.342	1.010
April 30	0.635	0.386	1.021
May 7	0.606	0.410	1.026

A sample of solution was obtained from a drug store, the solution being at least two years old and showing a marked red color. This solution gave a positive test for free iodine both with starch test solution and with $CHCL_3$. A sample of the same solution decolorized with $Na_2S_2O_3.5H_2O$ V. S. was assayed as above with the following results:

Date	% AsI_3 actually present	% pentavalent arsenic calculated to AsI_3.	Total arsenic calculated to % AsI_3.
April 30	0.038	0.965	1.003

This shows that even in extremely old solutions where oxidation of the trivalent arsenic is almost complete the total arsenic content when calculated to AsI_3 remains practically constant.

Conclusions

The Assay for HgI_2.

(1) The U. S. P. X. assay consisting of reduction with HCHO in an alkaline solution followed by decantation of the supernatant liquid is modified by filtering the solution, thus preventing any loss of the reduced mercury by decantation.

Stability.

(2) As the per cent. of AsI_3 decreases with the production of H_3AsO_4, there is an increase in the acidity due to the H_3AsO_4 acting as a monobasic acid.

(3) The solution deteriorates rapidly regardless of conditions of storage, although samples exposed to light deteriorate slightly quicker than those kept in the dark, yet there is not sufficient difference in these rates of deterioration to warrant any unusual care in the storage of the solution.

(4) In a period extending over three months oxidation of as much as 60 per cent. of the AsI_3 was noted.

(5) The original AsI_3 content is obtainable by adding to the remaining AsI_3, also that represented by the oxidized arsenic.

(6) Only a very old solution with a reddish color gave a positive test for free iodine with both starch test solution and with $CHCL_3$, and in this sample only about 5 per cent. of the original AsI_3 content remained in the arsenous condition.

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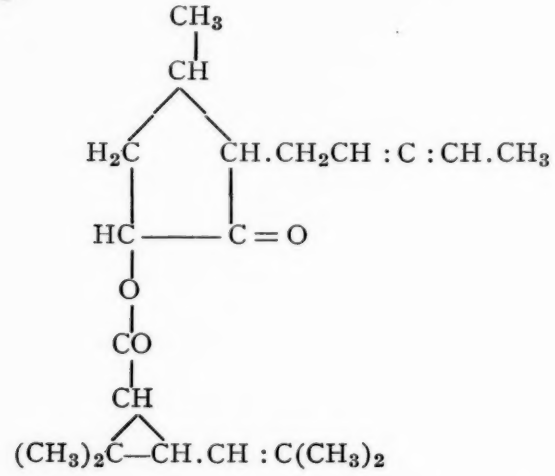
ABSTRACTED AND REPRINTED ARTICLES

PYRETHRUM AS AN INSECTICIDE*

IT HAS LONG been known that the flowers of certain species of chrysanthemum possess marked insecticidal powers. A Swiss author [1] reported in 1918 upon the successful cultivation of the plant from genuine imported seeds of *Pyrethrum cinerariæfolium* since 1912 and its use in combating the cochylis worm of the vine. Japanese workers [2] were early in the field, and in 1918 Ryo Yamamoto gave a detailed method for the isolation of the active principle of pyrethrum flowers, pyrethrone (the name first proposed by S. Sato). He found the greatest amount in the ovary, very little in the sepals, and a negligible quantity in the pollen, stigma and petals. He stated that pyrethrone was not a chemical individual but a mixture of substances, which on hydrolysis yield higher alcohols $C_{21}H_{34}O$ and $C_{27}H_{46}O$, one liquid fatty acid, palmitic acid and possibly another solid fatty acid. J. Chevalier [4] gave an account of pyrethrum as an insecticide in 1923, its activity and preparations made from it, and the previously mentioned Japanese author, R. Yamamoto, suggested in a further paper that the structure of the solid acid which he had obtained was HO_2. CCH. CMe_2. CHCH : CH Et. He named this pyrethronic acid. A. Juillet [6] described in 1923 an apparatus for continuous extraction and centrifuging of the extract in a current of steam. While this was not claimed to extract as completely as the Soxhlet, it was considered to be superior to percolation in the yield and in rapidity of action. Its significance resided in the fact that it was adapted to use on the commercial scale. Alcohol was found more efficient as the extracting medium than C_2HCl_3 and CCl_4. Staudinger and Ruzicka [7] in a very fine and comprehensive research controverted many of the statements of the Japanese investigators. They isolated two active principles, which they called pyrethrin I and pyrethrin II, and completely elucidated their chemical constitution. They found from 0.2 to 0.3 per cent. of the mixed pyrethrins in the flowers (subsequent investigators have found larger proportions) of which about 40 per cent. was pyrethrin I. This substance is several times as toxic to in-

*Reprinted from *The Chemist and Druggist.*

sects as pyrethrin II and is the most powerful insecticide known, dilutions of 1 to 10,000 being fatal to cockroaches in ten minutes. Both are esters of pyrethrolone (methyl pentadienylcyclopentanolen) with, in the first case, chrysanthemum mono-carboxylic acid (di-methyl-isobutenyl-trimethylene carboxylic acid) and in the second case chrysanthemum di-carboxylic acid (the mono-methyl ester of a closely-allied di-carboxylic acid), the constitutional formula for pyrethrin I being



They also synthesized a number of similar compounds, but found that none of them approached the pyrethrins in toxicity to insects, the slightest change in the constitution producing a great weakening in, or the disappearance of, the toxicity.

Cultivation on the Continent

It is of interest to note that the cultivation of pyrethrum continued to receive special attention on the Continent and a description of the process, preparations of pyrethrum and of the application of insecticides derived from it together with suggestions as to the extension of their use to other regions provided a very useful paper by A. Dufoux.[9] Investigations of Ziegler,[5] who studied pyrethrum from the pharmacological standpoint, found that common specimens gave from 3.81 per cent. to 6.85 per cent. of Et_2O extract. For tests an extract was prepared by percolation with the Et_2O and spontaneous evaporation of the solvent. This proved highly toxic to boll weevil either by

spray or in food. Frogs and turtles to which the drug was administered died. That great progress was being made with regard to the insecticidal value of pyrethrum is signified by the fact that in 1920 the U. S. Department of Agriculture gave official recognition to insecticides prepared from (1) *Chrysanthemum* (Pyrethrum) *sinerariæfolium,* (2) *Chrysanthemum* (Pyrethrum) *roseum,* Web. and Mohr, (3) *Chrysanthemum Marshallii Aschers* (syn. *Pyrethrum carneum,* M.B.). This formed an illuminating paper by McDonnell, Roark and Keenan,[8] who mentioned that the first is the only one found in commerce to any extent. It grows wild in Dalmatia, is cultivated there, in Japan and in California. The preparation of the powder is described in detail. Experimental work on the active insecticidal constituents of pyrethrum flowers showed the absence of alkaloids, and that the activity is due to mixture of acids and esters which are soluble in organic solvents, but insoluble in water. Events moved rapidly after this, and the standardization of pyrethrum by chemical and biological methods was discussed under Marsais,[10] in 1926. The agricultural requirements of pyrethrum and the manner of application for the eradication of common garden and house pests, such as caterpillars, aphides, fleas, etc., in general were adequately described by H. Staehelin.[11] Further advance was established by René Salomon,[20] who did work on soap-pyrethrum preparations and demonstrated their great toxicity, even at dilutions of 0.2. He showed that no objectionable residue remained on the crops and no injury to foliage resulted, even during the hottest time of the year. An effort to effect physiological standardization was made by Chevalier and Ripert,[12] who described the pharmacological action and physiological titrations of preparations of pyrethrum flowers and stated that frogs were killed by the extract of a good powder. It was found scarcely toxic to warm-blooded animals. In the absence of a chemical method they suggested physiological standardization of the drug by means of the frog. More progress regarding the chemistry of pyrethrum was effected by Tattersfield and Hobson,[15] who found that pyrethrin I and II, isolated according to the method of Staudinger and Ruzicka, were highly toxic to *Aphis rumicis.* Pyrethrin I was found about ten times as toxic as II, and is probably mainly responsible for the insecticidal value of the plant. Gnadinger and Corl [14] isolated pyrethrin I and II from Japanese pyrethrum flowers, and investigated their action on alkaline copper solution, and giving weights of pyrethrin I equivalent to amounts of dextrose from 0.750 to 2.875 mgm. Based on these

values a method is described for determining the percentage of active principles in pyrethrum flowers. The percentage ranged from 0.40 to 1.21 per cent. in the sixteen samples examined. The active principles of Japanese pyrethrum were found to be identical with those of the Dalmatian variety. They determined the toxicity of the pyrethrins to cockroaches, and found the pure pyrethrins extremely toxic to these insects. Staudinger and Harder [15] described two micro-analytical methods of determining the pyrethrin content (*a*) by means of the acid found on hydrolysis, (*b*) by means of the semicarbazone. The analytical methods were confirmed by results. Tattersfield and Gimingham [16] worked out a method for determining the pyrethrins based on Staudinger's method, but as that was long and tedious, subsequently devised a shorter method of determining pyrethrin I, which gives good results, and as pyrethrin I is so much more toxic than pyrethrin II, is sufficient for determining the strength of the flowers or their preparations.

Suitable Solvents

A large measure of success having attended the efforts of research workers on the chemical side, consideration was now increasingly bestowed upon the question of solvents and their practical advantages in application. McDonnell, Roark, Laforge and Keenan [17] found that chloroform, carbon tetrachloride, ethyl alcohol and benzene remove the active principles of pyrethrum, and Roark and Cotton [18] found butyl alcohols and isopropyl alcohol to be more toxic than methyl and ethyl alcohols in the vapor phase to rice weevils. On account of its combustibility, immiscibility and injurious action on plants, Gerstoff and Davidson [19] criticized the kerosene extract of pyrethrum. They gave a table showing the degree of extraction, toxicity and effect upon the host in the case of various solvents. Many of these were found perfectly harmless to the cabbage. The pyrethrum principle was extracted for practical use against the *Myzus Persicæ,* Sulz.[20] The use of powdered insect flowers particularly in horticulture has many disadvantages, largely on account of the pyrethrins being in the interior of the plant cells, and consequently do not readily come into contact with the insects. The employment of extracts also presents difficulties, as the pyrethrins readily hydrolyze and so lose their activity; this takes place particularly rapidly in the presence of alkali, and thus the use of soft soap, as has been recommended for emulsifying preparations of the flowers for the purpose of sprays, is undesirable. It is

interesting, in view of the extensive researches which have been carried out in this field by foreign workers, to learn that English manufacturers (Stafford Allen & Sons, Ltd.) have, as a result of experiments in their own laboratories and tests on their own farms, placed upon the market a pyrethrum insecticide under the name of Pysect, which has been granted the Award of Merit of the Royal Horticultural Society, 1929. This firm has also set aside a considerable acreage of their land for the experimental cultivation of the plant. This has overcome the disadvantages of other preparations, as it is stable, forms a good emulsion by merely mixing with water, and is non-poisonous. It is a most effective insecticide, and should for ordinary garden or agricultural purposes supersede quassia, nicotine and the older washes. Pyrethrum forms the basis of most of the sprays now on the market for killing house-flies, etc. These have become very popular, particularly in hot climates. It may be mentioned that the same manufacturers supply a concentrated liquid extract of pyrethrum which on dilution with paraffin produces a highly efficient fly-killing spray for use in rooms and stables.

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MEDICAL AND PHARMACEUTICAL NOTES

WARNING AGAINST FALSE HOPES OF CANCER CURE—For the second time within a month, the *Journal of the American Medical Association* has warned physicians and the public not to place undue faith in new methods of treating cancer by glandular extracts, such as that recently announced by Drs. W. B. Coffey and J. D. Humber of San Francisco.

Drs. Coffey and Humber themselves have insisted that their work is still in the experimental stage.

"We do not claim to treat or cure cancer," they stated in a telegram to the American Medical Association.

Dr. Boris Sokoloff, who has developed a method which uses a combination of extract from the cortex of the suprarenal glands and iron salt, has confined himself to laboratory investigations so far.

"My personal activity was and is limited strictly to experimental investigation carried out in the laboratory and so far I have not treated patients and do not intend to do so in the future," Dr. Sokoloff has reported to the American Medical Association.

Two other investigators have reported to the American Medical Association experiments with methods of treating cancer. Dr. C. F. Charlton, of Pasadena, Calif., has found a way to destroy cancer cells with administration of extract from the omentum, a membrane which goes from the stomach to adjacent organs. Dr. Adolph M. Hanson, of Faribault, Minn., announced similar results, using an extract from the thymus gland. Many other manuscripts describing the use of glandular extracts or tissues in the treatment of cancer have been received by the American Medical Association since the Coffey-Humber method has been made public.

Without criticizing the work of any of these investigators, the editors of the Association's *Journal* point out that "modern discoveries are the results of the accumulation of investigations over a series of years pointing towards a definite end." But until that end has been reached and the success of the newly-discovered method established beyond doubt, the public should not seek immediate practical applications of the method.

"When thousands of sufferers from cancer are led to false hopes, when husbands mortgage homes in order to carry wives with incurable

cancer across the continent for experimentation with unestablished methods, the *Journal* must continue to caution physicians and the public," the editorial concludes.

GERMS HAVE INVISIBLE STAGES—Scientists have often been baffled in their search for disease germs because germs have a stage or stages of development in which they are too small to be recognized by microscopic examination, filtrable through fine filters and, for a time at least, non-cultivable by ordinary methods. This is the opinion of Dr. Philip Hadley of the Medical School of the University of Michigan.

Dr. Hadley, internationally known for his studies on the curious transformations which bacteria undergo in artificial cultures and in the body, told a gathering of scientists that he had been successful repeatedly in causing disease-producing bacteria, appearing under the microscope and in cultures in the conventional form, to undergo dissociative changes which rendered them invisible, and filtrable through fine-grained earthen and porcelain filter candles. After further laboratory procedures these minute bodies were made to re-develop into the "normal" form. Sometimes weeks or months were required to effect this reversion.

Should Dr. Hadley's experiments and conclusions be correct—and it was admitted that it was more than possible that they were—a number of firmly held notions in present-day bacteriology would seem to demand some revision. This referred to such matters as valid criteria for judging the sterility of normal or pathological tissues and body fluids, criteria for judging when a bacterial culture was really dead, the true significance of so-called "bacteriolysis" and the bacteriophage phenomenon; also perhaps, the biological relation between the filtrable forms of bacteria and some of the so-called filtrable viruses.

Dr. Hadley emphasized the need of studying bacteria not alone with reference to the ordinary form that is well known to bacteriologists and described in the textbooks, but also with reference to the other cyclostages in which the organisms may masquerade for a time, and in which form they are seldom recognized. One of the most important of these is the filtrable form which occurs in the G-type culture.

The speaker voiced the opinion that, contrary to the common belief, any bacterial species in its entirety is not so simple a thing

that it can be revealed by a study of a single cell or a single culture; but that it is highly intricate in its cellular organization. This might be taken to mean that far more remains to be discovered regarding the complex biology of many "well-known" microbes than is already known by bacteriologists today.—(*Science Service.*)

ACIDIMETRIC ESTIMATION OF CORROSIVE SUBLIMATE TABLETS—The frequency of the application of analytical control methods depends a great deal on the simplicity and ease with which they can be carried out. In volumetric analysis this applies especially to processes requiring only one cheap and stable normal solution. As N-HCl and N/10-HCl come up to this standard, as many estimations as possible should be done acidimetrically. On these considerations the two corrosive sublimate estimations described hereafter are based. (1) KCN is added to a solution of $HgCl_2$, and the excess of KCN is titrated back with N/10-HCl. There is, however, no official standard for KCN. (2) $HgCl_2$ is reduced with N/10-alkali and H_2O_2; the excess of alkali is then titrated back with acid. N-alkali or N/10-alkali as required by this method are not very stable and require each time standardisation against N-CHl or N/10-HCl, which, in their turn, are standardised against $KHCO_3$. As this verification takes up much time, the idea suggested itself to use $KHCO_3$ direct for the titration, as it is cheap and can easily be obtained pure. One Gm. $KHCO_3$ requires for neutralisation exactly 10.011 cc. N-HCl, or practically 10 cc. Two Gms. $KHCO_3$ correspond to 20 cc. N-HCl, and are therefore equal to 20 cc. N-alkali. There is no difficulty for an experienced analyst to weigh out exactly 2 Gms. of the granular, non-hygroscopic salt on a small handscale with a margin of error up to $\pm$ 2 mgm. or $\pm$ 0.1 per cent. D. A. B. VI. has a specially purified $KHCO_3$ "pro analysi," prepared by precipitation from alcohol; the standard of the ordinary $KHCO_3$ D. A. B. VI. is, however, high enough for analytical purposes. To keep it ready for use, a quantity of the crystalline salt is reduced to coarse powder, dried at 60° or 70° C. or in the desiccator, and stored in well-closed bottles over $CaCl_2$. It supplies a stable alkaii for titrations, of which—

2 Gms. = 20 cc. N-alkali = 20 cc. N-acid;
10 Gms. dissolved to 100 cc. correspond to N-alkali;
10 Gms. dissolved to 1000 cc. to N/10-alkali.

The estimation of corrosive sublimate tablets is carried out as follows: 2 Gms. $KHCO_3$ are exactly weighed out and dissolved in a spacious

beaker in 50 cc. H_2O; 5 cc. acid-free hydrogen peroxide solution (100 vol.) and one 2-Gm. or two 1-Gm. corrosive sublimate tablets are added and heated over a small flame with agitation to about 70° C., until the mercury and the absorbed colouring matter have settled down as a heavy grey sludge covered by the clear liquid. This takes a few minutes only. One has to make sure that any particles of mercuric oxide, which may have been carried through excessive agitation to the sides of the beaker, have been completely reduced; the walls of the beaker are then rinsed with about 30 cc. H_2O, and after cooling titration with N-HCl to pink is carried out, using 2 or 3 drops methyl orange as indicator. Not more than 12.8 and not less than 12.5 cc. should be required, which corresponds to 48.9 to 50.9 $HgCl_2$ (1 cc. N-alkali = 0.1357 Gm. $HgCl_2$). It is essential that the corrosive sublimate tablets are of neutral reaction and give a clear solution.—Prof. E. Rupp (*Zentralblatt fuer Pharmazie*, **25**, 42, 438 through *Pharm. Jour.*)

Cut Hospital Costs by Using Standard Drugs—If physicians would prescribe standard drugs instead of proprietary drugs for their patients in hospitals, they would help to cut the cost of hospital care for the patients, Dr. Ernest E. Irons, dean of Rush Medical College of the University of Chicago, advised the Congress on Medical Education and Hospitals meeting at their recent meeting.

Proprietary drugs are nearly always more expensive and yet no more effective. If a better product is sold under a trade name, the specification of that brand may be justified, but most of the trade-marked brands comply only with the fixed minimum standards of the U. S. Pharmacopœia, William Gray, pharmacist of the Presbyterian Hospital here, explained to the same gathering. The prescribing of many brands of the same drugs causes duplication of stock and ties up money that might be used to better advantage. He named a number of drugs which under copyrighted names sell for from two to nine times as much as under their official titles.

"The shelves in some hospital pharmacies remind one of the exhibits of proprietary medicines in a chain-drug-soda fountain-lunch-room," Dr. Irons declared.

A serious result of using drugs with widely advertised names is that patients tend to continue to use them without medical advice. Many drugs that are safe to use for short periods are dangerous if used in large doses over long periods, Dr. Irons pointed out. He told of one drug which in a number of cases had caused fatal damage to

the liver when patients had taken it on their own responsibility after leaving the hospital.

CANCER A BACTERIAL DISEASE—The Vienna botanist, Dr. Gustav Klein, has been asked by the I. G. Farben-Industrie in Ludwigshafen, manufacturers of chemicals, to take over the direction of its newly-created cancer institute, which is the largest in Europe. His special field will be researches on the etiology of cancer. In an address delivered last year before the Gesellschaft der Aerzte in Vienna, Professor Klein gave same startling information on plant cancer and the relations of plant cancer to cancer in man. He spent some time, last summer, at Ludwigshafen, where the firm afforded him the opportunity to continue his researches. He made known recently some of the results of those researches in an address before the Vienna Biologische Gesellschaft. Klein takes the stand that plant cancer such as occurs in roses. species of *Pelargonium,* certain varieties of beans, and in grapevines is identical with experimental mouse cancer. He has succeeded in securing from the cancer of plants a pure culture of the same bacillus that he obtained from the tumors of the mouse. While he has not yet been able to demonstrate this bacillus in a microscopic preparation, he has been able to find the same bacillus in cancer of the breast and cancer of the rectum, in man, and to grow therefrom a pure culture. In the large laboratory at Ludwigschafen, it will be his task to establish the etiology of cancer along this direction, and try in animal cancer and in human such remedies as he finds will heal plant cancer.—(From our regular Vienna correspondent, *Jour. A. M. A.,* Vol.94, No. 10, page 733.)

NEWS ITEMS AND PERSONAL NOTES

FOUNDER'S DAY, PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE—The 109th anniversary of the founding of the Philadelphia College of Pharmacy and Science was celebrated in the new building of the College on Monday afternoon and evening, February 24th, with a special program in the afternoon and an alumni reunion and entertainment in the evening.

The afternoon program began with an academic procession of the entire faculty and instructional staff of the College numbering now more than 50 persons.

The invocation was pronounced by the Reverend Dr. W. J. Miller, Jr., of the Tabernacle Lutheran Church, Philadelphia, followed by a welcome by President Wilmer Krusen. The address of the day was delivered by Dr. Theodore B. Appel, secretary of Health of the Commonwealth of Pennsylvania. Dr. Appel's address reviewed the early and parallel development of the professions of medicine and pharmacy and outlined the relations which should exist between the two professions for the greatest development of both.

The feature of the evening entertainment, which was under the auspices of the Alumni Association of the Philadelphia College, was an original dramatic sketch written by Dean Charles H. LaWall and Millicent R. LaWall, both graduates of the College and long identified with its affairs. The sketch was a clever dramatization of the vision of the 68 founders of the Philadelphia College who met in historic Carpenter's Hall, Philadelphia, on February 23, 1821, to plan there and create the first college course to be instituted in the United States for the professional training of pharmacists.

The cast was composed of the following alumni of the Philadelphia College:

Harvey P. Frank, 1913
William W. Stoneback, 1917
Ralph L. Calvert, 1921
Charles C. Pines, 1921
John E. Kramer, 1925
George W. Perkins, 1925
Morris G. Acton, 1926
Eugene Catteau, 1929
Edmund McLaughlin, 1929
Linwood F. Tice, 1929
Andrew H. Walsh, 1929
Paul C. Wiesman, 1929

The feminine parts in the sketch were played by Mrs. Ada S. Capwell, Librarian of the Philadelphia College, and Evelyn L. Card, head of the College bookstore and supply department.

More than 500 alumni and friends of the Philadelphia College were present at the afternoon and evening exercises. Alumni from New York, Atlantic City, Pittsburgh, Harrisburg, and many other cities at a considerable distance from Philadelphia, took this opportunity to revisit their Alma Mater in its new home.

Following the play, Mrs. Svere Gulbrandsen, of Woodbury, New Jersey, gave a short recital of songs popular at the time of the founding of the Philadelphia College. The rest of the evening was devoted to games and dancing.

DIAGNOSIS OF UNDULANT FEVER—Huddleson and his co-workers have developed the rapid agglutination test for the serum diagnosis of undulant fever. It affords the practitioner an accurate test, comparatively simple in technic, not requiring any expensive laboratory equipment.

The results are immediate with this improved test and when conducted with properly standardized antigen, is just as accurate as the "long" or test-tube method, according to the published reports of authorities.

The reliability and accuracy of the test is intimately related to the antigen employed. The reliability of Antigen-Huddleson is guaranteed, as each lot is standardized and passed by Dr. I. F. Huddleson.

Antigen-Huddleson is produced solely by the H. K. Mulford Company, Philadelphia, from whom descriptive and direction folder can be procured.

CANADIAN BRANCH, FRITZSCHE BROTHERS, INC.—Fritzsche Brothers, Inc., 78-84 Beekman Street, New York, N. Y., announce that their Canadian Branch, Fritzsche Brothers of Canada, Ltd., located at 93-95 Church Street, Toronto, Ontario, since 1923, will move on March 1st to 77-79 Jarvis Street, corner of Luke Street, Toronto, Ontario. The steady growth and remarkable progress of the Canadian Branch has made this change necessary to maintain the prompt and efficient service characteristic of Fritzsche Brothers, Inc., and its branches.

VENTRICULIN—Ventriculin is the name Parke, Davis & Company have adopted for a new antianemic substance, a desiccated stomach extract, which is announced as a specific in the treatment of pernicious anemia.

The new product is the result of researches collaborated in by Dr. E. A. Sharp of the Parke-Davis Department of Experimental Medicine and Drs. C. C. Sturgis and Raphael Isaacs of the Thomas Henry Simpson Memorial Institute for Medical Research of the University of Michigan, and each lot is tested by the institute before it is released for sale, thereby assuring the potency of the product.

Ventriculin is supplied in the form of a dry, granular, palatable substance, in 10-gram vials only, in packages of 12 and 25 vials.